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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/242,772	06/25/1999	WILLEM JAN MARIE VAN DE VEN	702-990278	1485

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EXAMINER

SPIEGLER, ALEXANDER H

ART UNIT

PAPER NUMBER

1656

DATE MAILED: 01/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/242,772

Applicant(s)

VAN DE VEN ET AL.

Examiner

Alexander H. Spiegler

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 November 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 28,29,32-35 and 47-49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 28,29,32-35 and 47-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This action is in response to Paper No. 21, filed on November 11th, 2001.

Currently, claims 28-29, 32-35, and 47-49 are pending.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 28-29, 32-35, and 47-49 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 28-29, 32-35, and 47-49 are indefinite over the recitation of "having" because it is not clear as to whether this refers to "open" (i.e. comprising) or "closed" (i.e. consisting of) claim language.

B) Claims 34 and 35 are indefinite over the recitation of "the derivative" because this recitation lacks antecedent basis.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 33-35 and 48-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. Applicants have amended the claims to recite "a **fusion** of at least two of an oligonucleotide, a polynucleotide, and a gene having a nucleotide sequence of at least

part of a T-gene”, however, this recitation is not found in the specification, and therefore, is considered to be new matter.

6. Claims 28-29, 32-35, and 47-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claimed invention is drawn to an isolated nucleic acid wherein the nucleic acid is one of oligonucleotide, a polynucleotide, and a gene having a sequence of at least part of the PLAG1 gene, a sequence complementary thereto, or antisense version of the nucleic acid, wherein a protein encoded by the nucleic acid comprises a polypeptide sequence which is at least 75% identical to a polypeptide of PLAG1 in the region from zinc fingers 4 to 7. The claims are also directed towards a macromolecule comprising at least part of the CTNNB1 gene and fusions thereof.

In Figure 4A of the specification, Applicant discloses the cDNA of the nucleotide sequence of the PLAG1 gene, and on page 41 of the specification, Applicant discloses genomic organization of the PLAG1 gene including regulatory regions, i.e. introns, exons, coding and non-coding regions. The specification fails to describe an isolated nucleic acid wherein the nucleic acid is one of oligonucleotide, a polynucleotide, and a gene having a sequence of at least part of the PLAG1 gene, a sequence complementary thereto, or antisense version of the nucleic acid, wherein a protein encoded by the nucleic acid comprises a polypeptide sequence which is at least 75% identical to a polypeptide of PLAG1 in the region from zinc fingers 4 to 7” or a macromolecule comprising “at least

part of the CTNNB1 gene and fusions thereof”, which encompasses a large genus and sequences that are not described or disclosed. Additionally, the specification fails to adequately describe the various nucleotide variations, such as substitutions, insertions, deletions, nonsense or frameshift mutations that are encompassed by the gene (and with respect to claims 28-29, degenerate sequences thereof). Each of the claimed invention is a genus for which a representative number of species for each genus must be disclosed to meet the written description requirement of 112, first paragraph. As set forth by the Court in *Vas Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, the written description must convey to one of ordinary skill in the art “with reasonable clarity” that as of the filing date applicant was in possession of the claimed invention. Absent a written description disclosing a representative number of species of the isolated nucleic acid and macromolecule of claims 28-29, 32-35, and 47-49 has not been demonstrated “with reasonable clarity” that applicant was, in fact, “in possession of the claimed invention” at the time the application for patent was filed.

7. Claims 28-29, 32-35, and 47-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the cDNA sequence of the PLAG1 gene, does not reasonably provide enablement for an isolated nucleic acid wherein the nucleic acid is one of oligonucleotide, a polynucleotide, and a gene having a sequence of at least part of the PLAG1 gene, a sequence complementary thereto, or antisense version of the nucleic acid, wherein a protein encoded by the nucleic acid comprises a polypeptide sequence which is at least 75% identical to a polypeptide of PLAG1 in the region from zinc fingers 4 to 7. The specification does not reasonably provide enablement for a nucleic acid having homology with the zinc finger domains of the

PLAG1 gene or the complementary strand thereof, including modified, degenerate, or elongated versions of both strands. Furthermore, the specification does not reasonably provide enablement macromolecule comprising at least part of the CTNNB1 gene and fusions thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue (See *In re Wands*, 858 F. 2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include, but are not limited to:

I. *Quality of Experimentation Necessary:*

The claimed invention is drawn to an isolated nucleic acid wherein the nucleic acid is one of oligonucleotide, a polynucleotide, and a gene having a sequence of at least part of the PLAG1 gene, a sequence complementary thereto, or antisense version of the nucleic acid, wherein a protein encoded by the nucleic acid comprises a polypeptide sequence which is at least 75% identical to a polypeptide of PLAG1 in the region from zinc fingers 4 to 7, and a macromolecule comprising at least part of the CTNNB1 gene and fusions thereof. At page 4 of the specification, the Applicant discloses the genomic organization of the PLAG1 gene including regulatory regions, i.e. introns, exons, coding and non-coding regions. Although members of the PLAG1 gene family have been cloned and characterized in the prior art, Applicant fails to describe an isolated nucleic acid having a sequence comprising a part of the PLAG1 gene, gene comprising part of the

PLAG1 gene, degenerate sequences thereof, or a macromolecule comprising at least a part of the CTNNB1 gene and fusions thereof. The specification does not disclose any of the various substitutions, insertions or deletions that are encompassed by the gene or degenerate sequences thereof. Additionally, the specification fails to provide information to enable one of ordinary skill in the art to make or use the claimed nucleic acid using the large number of undisclosed nucleotide variations encompassed by the claims. In the first example, the Applicant discloses directional chromosome walking studies wherein yeast artificial chromosome clones (YACs) are isolated and screened followed by methods of fluorescence *in situ* hybridization for chromosome mapping studies. In the second example and subsequent examples, the Applicant discloses identification of a member of the PLAG1 gene family using classical molecular biology techniques that are well known in the prior art. The examples also disclose wherein probes and primers specific for the PLAG1 gene are utilized in methods of amplification and blotting to detect regions of the PLAG1 gene associated with tumor formation and growth. Nowhere in the examples does the Applicant provide information to enable one of ordinary skill in the art to isolate a nucleic acid having a sequence comprising a part of the PLAG1 gene, gene comprising part of the PLAG1 gene, degenerate sequences thereof, or a macromolecule comprising at least a part of the CTNNB1 gene and fusions thereof. As to the quality of experimentation required, one of ordinary skill in the art would have to design an experimental procedure to isolate a nucleic acid wherein the nucleic acid sequence is an oligonucleotide, a polynucleotide and a gene having part of the PLAG1 gene (or CTNNB1 gene and fusions thereof) and degenerate sequences thereof that is commensurate with the entire scope of the claims.

II. Amount of Direction and Guidance

The specification does not provide to an isolated nucleic acid wherein the nucleic acid is one of oligonucleotide, a polynucleotide, and a gene having a sequence of at least part of the PLAG1 gene, a sequence complementary thereto, or antisense version of the nucleic acid, wherein a protein encoded by the nucleic acid comprises a polypeptide sequence which is at least 75% identical to a polypeptide of PLAG1 in the region from zinc fingers 4 to 7, or a macromolecule comprising at least part of the CTNNB1 gene and fusions thereof, that bears a reasonable correlation to the entire scope of the claims. The examples starting at page 11, lack information concerning how to isolate any PLAG gene or how to isolate an oligonucleotide, polynucleotide, or gene comprising a part of the PLAG1 gene or degenerate sequences thereof. The examples provided lack information concerning the size and composition of the nucleic acid sequence claimed to be associated with the PLAG1 gene or information concerning nucleotide variations encompassed by the degenerate sequences thereof. Furthermore, it is not clear what algorithms or parameters have been used to identify homology between the claimed nucleic acid sequence and the zinc finger domains of the PLAG1 gene, including modified, degenerate or elongated versions of both strands of the gene. Since the specification has not adequately identified the PLAG1 gene it cannot be determined whether the claimed isolated nucleic acid sequence is indeed a sequence comprising a part of the PLAG1 gene or some other gene. Therefore, the claimed invention provides insufficient guidance and directions for one skilled in the art to make and use the claimed invention without undue experimentation.

III. Presence and Absence of Working Examples

The specification of the claimed invention lacks proper working examples. Starting on page 11, the specification discloses isolation and analysis of YACs in chromosome walking studies. At page 32, the specification discloses general methods for identifying a member of the PLAG family in salivary glands. At page 53 and 54, Applicant discloses the identification of a PLAG2 gene using classical molecular biology techniques. Beginning at page 56, Applicants discloses a diagnostic test for pleomorphic adenomas of salivary glands using PLAG1-specific primers. At page 59, Applicant discloses a PLAG2 gene as a diagnostic marker for chromosome anomalies. At page 60, Applicant discloses the use of animal models involving PLAG1 as tools in *in vivo* therapeutic drug testing. The examples, however, fail to adequately disclose how to isolate the claimed nucleic acid sequence comprising at least a part of the PLAG1 gene or gene having a sequence comprising a part of the PLAG1 gene or degenerate sequences thereof. Merely making reference to the PLAG1 gene, probes and primers of the PLAG1 gene or PLAG2 gene as a member of the PLAG1 family as being encompassed in the instant invention does not enable the skilled practitioner to reproduce the results as reported in the specification.

IV. *Nature of the Invention*

The nature of the invention is an isolated nucleic acid wherein the nucleic acid is one of oligonucleotide, a polynucleotide, and a gene having a sequence of at least part of the PLAG1 gene, a sequence complementary thereto, or antisense version of the nucleic acid, wherein a protein encoded by the nucleic acid comprises a polypeptide sequence which is at least 75% identical to a polypeptide of PLAG1 in the region from zinc fingers 4 to 7, degenerate sequences thereof, and a macromolecule comprising at least part of the

CTNNB1 gene and fusions thereof. The full scope of the claimed invention is not reproducible due to the lack of guidance presented in the examples beginning at page 11. As noted, the specification does not properly disclose an isolated nucleic acid as one of a gene having a sequence comprising at least part of the PLAG1 gene, degenerate sequence thereof, or a macromolecule comprising at least part of the CTNNB1 gene and fusions thereof that bears a reasonable correlation to the entire scope of the claims.

V. Level of predictability in the art

The specification has not enabled an isolated nucleic acid as one of a gene having a sequence comprising at least part of the PLAG1 gene, degenerate sequence thereof, or a macromolecule comprising at least part of the CTNNB1 gene and fusions thereof.

Although certain relevant techniques useful to the claimed invention are known in the prior art, the prior art does not teach an isolated nucleic acid as set forth in the claimed invention.

Therefore, for all of the forgoing reasons, undue experimentation is necessary for one of skill in the art to obtain the claimed invention.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claim 33 is rejected under 35 U.S.C. 102(b) as being anticipated by Kraus et al. (Genomics (December 1994) 23: 272-274).

Claim 33 is drawn to a macromolecule comprising a nucleic acid isolated form, comprising one of an oligonucleotide, a polynucleotide and a gene having a nucleotide sequence of at least a part of a T-gene selected from the group consisting of the PLAG1 subfamily of zinc finger protein genes, and at least part of the CTNNB1 gene and fusions thereof, or complementary degenerate versions of the nucleotide sequence. Kraus et al. discloses this embodiment (pg. 272, column 2, last paragraph bridging column 1, pg. 273, lines 1-5, see also Fig. Legend 1).

10. Claims 33-35 are rejected under 35 U.S.C. 102(a) as being anticipated by Nollet et al. (Genomics (March 1996) 32: 413-424).

Claim 33 is drawn to a macromolecule comprising a nucleic acid isolated form, comprising one of an oligonucleotide, a polynucleotide and a gene having a nucleotide sequence of at least a part of a T-gene selected from the group consisting of the PLAG1 subfamily of zinc finger protein genes, and at least part of the CTNNB1 gene and fusions thereof, or complementary degenerate versions of the nucleotide sequence. Nollet et al. discloses this embodiment (pg. 418, bottom of column 1, bridging top of column 2, lines 1-24).

Claim 34 is drawn to an embodiment of claim 33, wherein the derivative is selected from the group consisting of : a) a transcript corresponding to the nucleic acid, b) cDNA corresponding to the nucleic acid, c) sense or antisense DNA corresponding to the nucleic acid, d) a nucleic acid including a gene, or a derivative thereof, isolated by using at least part of a gene as one of a probe or primer. Nollet discloses a macromolecule wherein the derivative is a nucleic acid including a gene, or a derivative thereof, isolated by using at least part of a T-gene as one of a probe or primer (pg. 414,

"Materials and Methods", lines 1-18 bridging top of column 2, lines 1-19). With respect to claim 35, the reference teaches that the derivative is labeled (pg. 414, column 2, lines 25-56 and 59-60).

Conclusion

11. No claims are allowable.

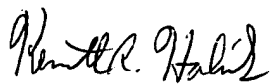
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Alexander H. Spiegler
January 28, 2002



KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

1/28/02